

## **REMARKS**

Claims 1-3, 5, 7, 10-20, 22-27, and 29 are pending in the present application, of which Claims 1-3, 7, 10-20, 23-26, and 29 are under consideration. Claims 1, 5, 7, 10, 16, 19, and 23 have been amended, and Claims 4 and 28 have been canceled. Support for the amendments may be found throughout the specification and original claims. As such, no new matter enters by way of the present claims. Entry of the present amendment and reconsideration of the application is therefore respectfully requested.

### **I. Election/Restriction Requirement**

Applicants acknowledge the finality of the election/restriction requirement. Further to the election, Claims 1-3, 7, 10-20, 23-26, and 29 are under consideration to the extent they read on the elected species. Claims 1-3, 5, 13-20, 22-26, and 29 are generic as to all species, while Claims 7, 10, 11, and 12 are under consideration to the extent they read on the elected species.

Upon allowance of a generic claim, Applicants reserve the right to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR § 1.141.

### **II. Rejection Under 35 U.S.C. § 103**

*Claims 1-4, 7, and 10-20*

Claims 1-4, 7, and 10-20 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Van West *et al.* (hereinafter, Van West) in view of Sanchez *et al.* (US 2004/0192764, hereinafter Sanchez) and Lanza *et al.* (US 5,912,005, hereinafter Lanza). Applicants respectfully traverse this rejection for at least the reasons that follow.

The Supreme Court recently addressed the issue of obviousness in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007). The Court stated that the *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), factors control an obviousness inquiry. Those factors are: 1) “the scope and content of the prior art”; 2) the “differences between the prior art and the claims”; 3) “the level of ordinary skill in the pertinent art”; and 4) objective evidence of

nonobviousness. *KSR*, 127 S. Ct. at 1734 (quoting *Graham*, 383 U.S. at 17-18). While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation (“TSM”) test in an obviousness inquiry, the Court acknowledged the importance of identifying “a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does” in an obviousness determination. *KSR*, 127 S. Ct. at 1731. Moreover, the Court indicated that there is “no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis.” *Id.* As long as the test is not applied as a “rigid and mandatory” formula, that test can provide “helpful insight” to an obviousness inquiry. *Id.* In this regard, “[r]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning **with some rational underpinning** to support the legal conclusion of obviousness.” *KSR*, 127 S.Ct. at 1741 (quoting *In re Kahn* 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added)).

In rejecting the claims, the Office alleges that it would have been obvious to a person of skill in the art “to employ the compounds of Van West et al. to contain citalopram and ibuprofen because the compounds of Sanchez et al. teach citalopram and the compounds of Lanza et al. teach ibuprofen and according to Van West et al, antidepressants, which act as anti-inflammatory agents, can be used to treat major depression and according to Lanza et al, ibuprofen is present in a composition that is used to treat major depression.” Office Action mailed November 15, 2007 at page 4. The Office further supports the rejection, stating that it is obvious “to combine individual compositions taught to have the same utility to form a new composition of the very same purpose”, and “to combine two compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose.” Applicants respectfully disagree.

The presently claimed invention, to the extent under consideration, is generally drawn to methods involving the treatment or alleviation of depression, the potentiation of the action of an antidepressant agent in a subject suffering from depression, or the treatment or prevention of

drug-induced depression in a subject suffering therefrom. In all instances, the methods include the administration of an amount of an anti-inflammatory agent effective to treat or alleviate depression, wherein the anti-inflammatory agent includes an NSAID.

Whatever else the cited references may disclose, there is no teaching or suggestion of the administration of an anti-inflammatory agent including an NSAID in an amount effective to treat or alleviate depression to a subject in need thereof. The alleged teachings in Lanza concerning the use of ibuprofen in methods of treating depression are misplaced.

Lanza teaches a method of implanting a living donor cell into a host animal without inflammatory response or rejection of the donor cell by the host animal, by obtaining an uncoated particle of a biocompatible, temperature-independent gel that encapsulates the living donor cell. The uncoated particle provides a molecular weight cutoff that prevents host animal immune cells from entering the particle, yet does not have to prevent entry of host animal IgG and complement into the particle, and implanting the uncoated particle into the host animal. See Lanza Abstract. Lanza discusses that uncoated gel beads containing cells that secrete neurotransmitters, e.g., 5-hydroxyindol acetic acid (5-HIAA), dopamine, gamma-aminobutyric acid (GABA), are useful to treat mood disorders and deficiencies, such as major depression. See Lanza, Col. 18, lines 28-44.

Lanza goes on to teach that the immune system of the host can also be modulated prior to or after implantation of the encapsulated donor cells to ensure survival of the implanted cells. “Allografts in mammals larger than mice or rats require a short course of an immunosuppressant or anti-inflammatory drug at a low dosage. Discordant xenografts with small beads, e.g., 700 to 900  $\mu\text{m}$  in diameter, in larger mammals such as humans also require adjunctive immunosuppression. As discussed below, minimal or no immunosuppression or anti-inflammatory therapy is necessary with larger beads.” Lanza, Col. 9, lines 46-56. In connection with these teachings of immune modulation, Lanza discloses that “[i]mmunosuppressant drugs include cyclosporine A (“CsA”), FK-506, and deoxyspergualin. Anti-inflammatory/anti-fibrosis

drugs include steroidal drugs such as prednisone, and non-steroidal drugs such as ibuprofen and aspirin.” Lanza, Col. 9, lines 57-61.

As such, Lanza does not in fact teach or suggest the use of ibuprofen in an amount effective to treat or alleviate depression. Rather, those skilled in the art, upon reading Lanza, would understand the disclosure of Lanza to teach the use of immune modulation in connection with allograft therapy under specified conditions, and only where appropriate (i.e., low dosages with small beads). However, in the absence of allograft therapy, there are no teachings in the cited prior art to lead those of skill in the art to the use of ibuprofen in the methods as presently claimed. There simply is no rational underpinning to support a predictable expectation that ibuprofen would be useful in the treatment or alleviation of depression itself, or any predictable expectation as to the administration of an amount of ibuprofen to a subject in need thereof effective in this regard.

Thus, contrary to the Office’s assertions, the ibuprofen of Lanza does not have the same utility for the same purpose as the compositions in Van West and/or Sanchez. Moreover, the allograft implantation techniques of Lanza are substantially different from the non-biological, non-invasive approaches of Van West and Sanchez. As such, those of skill in the art would not routinely look to combine the cell-based compositions of Lanza with the compositions of Van West and/or Sanchez.

For at least these reasons, withdrawal of the present rejection is respectfully requested.

*Claims 23-26 and 28-29*

Claims 23-26 and 28-29 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Anisman *et al.* (hereinafter Anisman) in view of Van West, Sanchez and Lanza. Applicants respectfully traverse this rejection for at least the reasons that follow.

As discussed above, whatever else the cited references may disclose, there is no teaching or suggestion of the administration of an anti-inflammatory agent including an NSAID in an

amount effective to treat or alleviate depression to a subject in need thereof. Anisman does nothing to remedy this deficiency.

For at least these reasons, and the reasons discussed above, withdrawal of the present rejection is respectfully requested

### **Conclusion**

In view of the foregoing amendments and remarks, applicant respectfully requests withdrawal of the outstanding rejections and timely allowance of the pending claims. If the Examiner believes that a telephone conference would be useful in resolving any outstanding issues, he is encouraged to call applicant's undersigned representative at (303) 863-2303.

Respectfully submitted,

/Milan M. Vinnola/

Milan M. Vinnola (Reg. No. 45,979)

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ARNOLD & PORTER LLP  
Attn: IP Docketing  
555 Twelfth Street, NW  
Washington, D.C. 20004-1206  
(202) 942-5000 telephone  
(202) 942-5999 facsimile